GenCore version 4.5
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OM protein - protein search, using sw model

Run on: July 10, 2002, 08:22:08 ; Search time 30.1 Seconds
(without alignments)
59.043 Million cell updates/sec

Title: US-09-508-054-19
Perfect score: 87
Sequence: 1 YLRIVQCRSVEGSCGF 16

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 747574 seqs, 111073796 residues

Total number of hits satisfying chosen parameters: 747574

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 150 summaries

Database : A_Geneseq_032802:*
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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	87	100.0	16	20	AAY01663	Peptide analogue 9
2	87	100.0	16	22	AAB73624	Human growth hormo
3	84	96.6	191	13	AAR24050	hGH variant #2 - 1
4	84	96.6	191	13	AAR24052	hGH variant #4 - 1
5	84	96.6	191	13	AAR24053	hGH variant #5 - 1
6	84	96.6	191	13	AAR24055	hGH variant #7 - 1
7	84	96.6	191	13	AAR24057	hGH variant #9 - 1
8	84	96.6	191	13	AAR24725	hGH variant #13 -
9	84	96.6	191	13	AAR24726	hGH variant #14 -
10	84	96.6	191	13	AAR24727	hGH variant #15 -
11	84	96.6	191	13	AAR24729	hGH variant #17 -
12	84	96.6	191	13	AAR24731	hGH variant #19 -
13	84	96.6	191	13	AAR24734	hGH variant #22 -
14	84	96.6	191	13	AAR24737	hGH variant #25 -
15	84	96.6	191	13	AAR24740	hGH variant #28 -
16	84	96.6	191	13	AAR24743	hGH variant #31 -
17	84	96.6	191	13	AAR24751	hGH variant #39 -
18	84	96.6	191	13	AAR24753	hGH variant #41 -
19	84	96.6	191	13	AAR24757	hGH variant #45 -
20	84	96.6	191	13	AAR24762	hGH variant #50 -
21	84	96.6	191	13	AAR24766	hGH variant #54 -
22	84	96.6	191	13	AAR24769	hGH variant #57 -
23	84	96.6	191	13	AAR24770	hGH variant #58 -
24	84	96.6	191	13	AAR24776	hGH variant #64 -
25	83	95.4	25	21	AAY78432	Human growth hormo
26	83	95.4	56	5	AAP40352	Synthetic human gr
27	83	95.4	65	22	ABB23044	Protein #5043 enco
28	83	95.4	65	22	AAM31150	Peptide #5187 enco
29	83	95.4	176	18	AAW26202	20 kDa human growt
30	83	95.4	176	18	AAW26203	20 kDa human growt
31	83	95.4	176	18	AAW23662	Authentic 20-kilod
32	83	95.4	176	18	AAW23661	Authentic 20-kilod
33	83	95.4	176	19	AAW59762	Amino acid sequenc
34	83	95.4	176	19	AAW59761	Amino acid sequenc
35	83	95.4	177	16	AAR76820	hGHV-3(53) growth
36	83	95.4	190	21	AAY84644	Amino acid sequenc
37	83	95.4	191	7	AAP60016	Sequence of human
38	83	95.4	191	13	AAR24754	hGH variant #42 -
39	83	95.4	191	13	AAR24772	hGH variant #60 -
40	83	95.4	191	18	AAW38221	Human growth hormo
41	83	95.4	191	18	AAW38222	Human growth hormo
42	83	95.4	191	18	AAW38220	Human growth hormo
43	83	95.4	191	19	AAW71289	Human growth hormo
44	83	95.4	191	20	AAY15809	Primary amino acid
45	83	95.4	191	20	AAY15810	Tagged human growt
46	83	95.4	191	20	AAY04396	Natural human 22kD
47	83	95.4	191	20	AAY04397	Mutant human 22kDa
48	83	95.4	191	22	AAB19836	Human growth hormo
49	83	95.4	192	10	AAP90129	Human growth hormo
50	83	95.4	192	20	AAW92266	Human anti-angioge
51	83	95.4	192	20	AAW92264	Human anti-angioge
52	83	95.4	192	22	AAB19835	Recombinant Ala-hu
53	83	95.4	193	8	AAP70260	Met-Asp-human grow
54	83	95.4	194	20	AAY30530	Recombinant human
55	83	95.4	198	16	AAR76819	hGHV-2(88) growth
56	83	95.4	202	21	AAY93637	Amino acid sequenc
57	83	95.4	203	15	AAR49815	20K hGH (42Met).
58	83	95.4	212	7	AAP60234	Sequence of AP sig
59	83	95.4	214	7	AAP60232	Sequence of Escher
60	83	95.4	214	7	AAP60233	Sequence of Escher
61	83	95.4	214	11	AAR05043	Human growth hormo
62	83	95.4	214	18	AAW10425	Synthetic human gr
63	83	95.4	214	20	AAY31766	Human growth hormo
64	83	95.4	214	20	AAW82801	Human growth hormo
65	83	95.4	214	21	AAY78424	Human growth hormo
66	83	95.4	214	21	AAY78460	Human growth hormo
67	83	95.4	217	4	AAP30046	Sequence of human
68	83	95.4	217	8	AAP71058	Sequence of human
69	83	95.4	217	11	AAR05169	Human growth hormo
70	83	95.4	217	15	AAR60516	Human somatotropin
71	83	95.4	217	16	AAR76818	Human growth hormo
72	83	95.4	217	19	AAW68453	Human growth hormo
73	83	95.4	217	21	AAB26769	Secretory cell pro
74	83	95.4	217	22	AAE10340	Human growth hormo
75	83	95.4	217	22	AAB35428	Secretory cell lin
76	83	95.4	226	15	AAR49814	20K hGH (42Ser).
77	83	95.4	241	20	AAW88526	Fusion of killer t
78	83	95.4	244	12	AAR10042	Plasmid pOW885 hum
79	83	95.4	245	21	AAY69791	MWPsp-MWPmp20-(His
80	83	95.4	344	22	AAB70473	Npro-hGH fusion pr
81	83	95.4	407	22	AAB49195	Human growth hormo
82	83	95.4	779	18	AAW22719	Human serum albumi
83	83	95.4	784	18	AAW22717	Human serum albumi
84	83	95.4	789	18	AAW22718	Human serum albumi

85	83	95.4	794	18	AAW22720	Human serum albumi
86	82	94.3	191	13	AAR24732	hGH variant #20 -
87	81	93.1	191	13	AAR24058	hGH variant #10 -
88	80	92.0	15	17	AAY01512	Human growth hormo
89	80	92.0	15	17	AAW02650	Human growth hormo
90	80	92.0	15	20	AAY01653	Peptide analogue o
91	80	92.0	15	20	AAY01655	Peptide analogue o
92	80	92.0	15	20	AAY01656	Peptide analogue o
93	80	92.0	15	20	AAY01658	Peptide analogue 9
94	80	92.0	15	20	AAY01659	Peptide analogue 9
95	80	92.0	15	20	AAY01679	Peptide analogue o
96	80	92.0	15	20	AAY01681	Peptide analogue o
97	80	92.0	15	20	AAY01660	Peptide analogue 9
98	80	92.0	16	20	AAY01664	Peptide analogue 9
99	80	92.0	17	20	AAY01654	Peptide analogue o
100	80	92.0	17	20	AAY01665	Peptide analogue 9
101	80	92.0	98	22	AAO06818	Human polypeptide
102	80	92.0	191	13	AAR24268	Mature human growt
103	80	92.0	191	13	AAR24269	Mature human growt
104	80	92.0	191	13	AAR24270	Mature human growt
105	80	92.0	191	13	AAR24271	Mature human growt
106	80	92.0	191	13	AAR24272	Mature human growt
107	80	92.0	191	13	AAR24049	hGH variant #1 - 1
108	80	92.0	191	13	AAR24051	hGH variant #3 - 1
109	80	92.0	191	13	AAR24054	hGH variant #6 - 1
110	80	92.0	191	13	AAR24728	hGH variant #16 -
111	80	92.0	191	20	AAY31765	Human placental la
112	80	92.0	191	22	AAB49196	Growth hormone act
113	80	92.0	191	22	AAB49197	Growth hormone act
114	80	92.0	191	22	AAB49198	Growth hormone act
115	80	92.0	191	22	AAB49199	Growth hormone act
116	80	92.0	192	20	AAW92262	Human anti-angioge
117	80	92.0	214	13	AAR22230	Human growth hormo
118	79	90.8	191	13	AAR24056	hGH variant #8 - 1
119	79	90.8	191	13	AAR24730	hGH variant #18 -
120	79	90.8	191	13	AAR24733	hGH variant #21 -
121	79	90.8	191	13	AAR24736	hGH variant #24 -
122	79	90.8	191	13	AAR24738	hGH variant #26 -
123	79	90.8	191	13	AAR24739	hGH variant #27 -
124	79	90.8	191	13	AAR24741	hGH variant #29 -
125	79	90.8	191	13	AAR24742	hGH variant #30 -
126	79	90.8	191	13	AAR24744	hGH variant #32 -
127	79	90.8	191	13	AAR24747	hGH variant #35 -
128	79	90.8	191	13	AAR24749	hGH variant #37 -
129	79	90.8	191	13	AAR24750	hGH variant #38 -
130	79	90.8	191	13	AAR24752	hGH variant #40 -
131	79	90.8	191	13	AAR24755	hGH variant #43 -
132	79	90.8	191	13	AAR24756	hGH variant #44 -
133	79	90.8	191	13	AAR24760	hGH variant #48 -
134	79	90.8	191	13	AAR24764	hGH variant #52 -
135	79	90.8	191	13	AAR24765	hGH variant #53 -
136	79	90.8	191	13	AAR24767	hGH variant #55 -
137	79	90.8	191	13	AAR24768	hGH variant #56 -
138	79	90.8	191	13	AAR24771	hGH variant #59 -
139	79	90.8	191	13	AAR24773	hGH variant #61 -
140	79	90.8	191	13	AAR24774	hGH variant #62 -
141	79	90.8	191	13	AAR24775	hGH variant #63 -
142	78	89.7	176	9	AAP82720	Human 20K growth h
143	78	89.7	191	13	AAR24748	hGH variant #36 -
144	78	89.7	191	13	AAR24758	hGH variant #46 -
145	78	89.7	191	13	AAR24761	hGH variant #49 -
146	78	89.7	191	20	AAW86013	Human growth hormo
147	78	89.7	191	21	AAY78425	Human growth hormo
148	78	89.7	191	22	AAB49200	Growth hormone act
149	78	89.7	191	22	AAB49201	Growth hormone act
150	77	88.5	15	20	AAY01661	Peptide analogue 9

ALIGNMENTS

RESULT 1
AAY01663

ID AAY01663 standard; peptide; 16 AA.
XX
AC AAY01663;
XX
DT 23-JUN-1999 (first entry)
XX
DE Peptide analogue 9604 of carboxy terminal sequence of hGH.
XX
KW Peptide analogue; human growth hormone; hGH; fat-reducing enzyme;
KW hormone-sensitive lipase; fat-producing enzyme; acetyl CoA carboxylase;
KW obesity; meat quality.
XX
OS Synthetic.
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 7..14
XX
PN WO9912969-A1.
XX
PD 18-MAR-1999.
XX
PF 04-SEP-1998; 98WO-AU00724.
XX
PR 13-NOV-1997; 97AU-0000398.
PR 08-SEP-1997; 97AU-0009001.
XX
PA (META-) METABOLIC PHARM LTD.
XX
PI Jiang W, Ng FM;
XX
DR WPI; 1999-229224/19.
XX
PT Peptide analogues of the C-terminus of a growth hormone
XX
PS Claim 16; Page 50; 95pp; English.
XX
CC The present sequence represents a peptide analogue of the carboxy
CC terminal (amino acids 177-191) of human growth hormone (hGH).
CC The peptide analogues can act to stimulate the fat-reducing enzyme
CC hormone-sensitive lipase and inhibit the fat-producing enzyme
CC acetyl CoA carboxylase, both effects being the result of activating
CC production of the second messenger diacylglycerol. The peptide
CC analogues are used to treat obesity, particularly in humans but
CC also to improve meat quality in farm animals.
XX
SQ Sequence 16 AA;

Query Match 100.0%; Score 87; DB 20; Length 16;
Best Local Similarity 100.0%; Pred. No. 1.1e-06;
Matches 16; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
||||||||||||||||
Db 1 ylrivqcrsvegscgf 16

RESULT 2
AAB73624
ID AAB73624 standard; peptide; 16 AA.
XX
AC AAB73624;
XX
DT 29-AUG-2001 (first entry)
XX
DE Human growth hormone fragment analogue peptide, AOD9604.
XX
KW Human growth hormone analogue peptide; hGH; AOD9604; lipid metabolism;
KW modulation; lipolysis stimulation; hormone-sensitive lipase stimulation;
KW lipogenesis inhibition; acetyl CoA carboxylase inhibition; obesity;
KW functional food; transgenic yeast; fat/lean ratio; food use;
KW cyclic.

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XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  7..14
XX
PN   WO200133977-A1.
XX
PD   17-MAY-2001.
XX
PF   06-NOV-2000; 2000WO-AU01362.
XX
PR   05-NOV-1999;   99AU-0003875.
XX
PA   (META-) METABOLIC PHARM LTD.
XX
PI   Belyea CI,  Ng FM,  Vaughan P;
XX
DR   WPI; 2001-328876/34.
XX
PT   New organisms containing nucleic acid encoding a growth hormone
PT   fragment which modulates lipid metabolism are useful to produce dietary
PT   aids for obesity and in the meat production industry  -
XX
PS   Example; Page 32; 54pp; English.
XX
CC   The invention relates to novel transgenic organisms useful in the
CC   production of functional food and drink products for the treatment
CC   or prevention of obesity via the regulation of lipid metabolism. The
CC   organisms comprise a polynucleotide encoding a growth hormone fragment
CC   capable of stimulating the activity of hormone-sensitive lipase (the key
CC   enzyme in lipolysis) and inhibiting acetyl CoA carboxylase (the key
CC   enzyme in lipogenesis). The growth hormone fragment preferably contains
CC   at least the disulphide-bonded loop of a mammalian growth hormone (but is
CC   not the full-length growth hormone) and is optionally linked to an
CC   epitope tag or heterologous fusion protein partner. The transgenic
CC   organism may be a microorganism used to produce a fermented product
CC   (e.g., yeast), or an edible plant or animal or cell thereof. Food or
CC   drink made using methods of the invention are used to modify fat/lean
CC   ratio, lipid metabolism or food use in a mammal. In particular, the food
CC   or drink products may be used to treat or prevent obesity, particularly
CC   in humans, and may also be used to improve the fat/lean ration of
CC   livestock raised for meat production. In the exemplification of the
CC   invention, the human growth hormone (hGH) fragment analogue AOD9604 was
CC   expressed in yeast, optionally fused to the FLAG epitope (AAB73625).
CC   The present sequence represents AOD9604, which corresponds to Tyr-hGH
CC   177-191.
XX
SQ   Sequence   16 AA;


  Query Match             100.0%;  Score 87;  DB 22;  Length 16;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-06;
  Matches   16;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||||||||||||||
Db      1 ylrivqcrsvegscgf 16


RESULT   3
AAR24050
ID   AAR24050 standard; Protein; 191 AA.
XX
AC   AAR24050;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #2 - 172Arg 174Ala 176Tyr 178Arg.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   4
AAR24052
ID   AAR24052 standard; Protein; 191 AA.
XX
AC   AAR24052;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #4 - 172Arg 174Ser 176Tyr 178Arg.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
```

```
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   5
AAR24053
ID   AAR24053 standard; Protein; 191 AA.
XX
AC   AAR24053;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #5 - 172Lys 174Ala 176Tyr 178Arg.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   6
AAR24055
ID   AAR24055 standard; Protein; 191 AA.
XX
AC   AAR24055;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #7 - 172Lys 174Gln 176Tyr 178Arg.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;
```

```
  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:||||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   7
AAR24057
ID   AAR24057 standard; Protein; 191 AA.
XX
AC   AAR24057;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #9 - 172Gln 174Arg 176Tyr 178Arg.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:||||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   8
AAR24725
ID   AAR24725 standard; Protein; 191 AA.
XX
AC   AAR24725;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #13 - 10His 14Gly 18Asn 21Asn.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:||||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT   9
AAR24726
ID   AAR24726 standard; Protein; 191 AA.
XX
AC   AAR24726;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #14 - 10Ala 14Trp 18Asp 21Asn.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
```

PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
|||||:|||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 10
AAR24727
ID AAR24727 standard; Protein; 191 AA.
XX
AC AAR24727;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #15 - 10Phe 14Ser 18Phe 21Leu.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
|||||:|||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 11
AAR24729
ID AAR24729 standard; Protein; 191 AA.
XX
AC AAR24729;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #17 - 10Ile 14Asn 18Ile 21Asn.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC Some of these hGH variants have stronger affinities for the hGH

```
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match            96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT  12
AAR24731
ID   AAR24731 standard; Protein; 191 AA.
XX
AC   AAR24731;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #19 - 174Ser 176Tyr 167Glu 171Ser 175Thr 179Ile.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match            96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT  13
AAR24734
ID   AAR24734 standard; Protein; 191 AA.
XX
AC   AAR24734;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #22 - 174Ser 176 Tyr 167Arg 171Asp 175Ile 179Ile.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match            96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT  14
AAR24737
ID   AAR24737 standard; Protein; 191 AA.
XX
AC   AAR24737;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #25 - 174S 176Y 10H 14G 18N 21N 167E 171S 175T 179I.
```

```
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           ||||:|||||||||||
Db     176 ylrimqcrsvegscgf 191


RESULT  15
AAR24740
ID   AAR24740 standard; Protein; 191 AA.
XX
AC   AAR24740;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #28 - 174S 176Y 10A 14W 18D 21N 167E 171S 175T 179I.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           ||||:|||||||||||
Db     176 ylrimqcrsvegscgf 191


RESULT  16
AAR24743
ID   AAR24743 standard; Protein; 191 AA.
XX
AC   AAR24743;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #31 - 174S 176Y 10F 14S 18F 21L 167E 171S 175T 179I.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
```

XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
|||||:||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 17
AAR24751
ID AAR24751 standard; Protein; 191 AA.
XX
AC AAR24751;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #39 - 174S 176Y 10A 14S 18T 21N 167R 171D 175T 179I.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
|||||:||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 18
AAR24753
ID AAR24753 standard; Protein; 191 AA.
XX
AC AAR24753;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #41 - 174S 176Y 10W 14G 18S 21S 167R 171D 175T 179I.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by digestion of each of the one-helix

CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
||||:|||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 19
AAR24757
ID AAR24757 standard; Protein; 191 AA.
XX
AC AAR24757;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #45 - 174S 176Y 10P 14S 18D 21N 167R 171D 175T 179I.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;
Best Local Similarity 93.8%; Pred. No. 3.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
||||:|||||||||||
Db 176 ylrimqcrsvegscgf 191

RESULT 20
AAR24762
ID AAR24762 standard; Protein; 191 AA.
XX
AC AAR24762;
XX
DT 08-DEC-1992 (first entry)
XX
DE hGH variant #50 - 174S 176Y 10A 14W 18D 21N 167R 171D 175T 179I.
XX
KW humanised IgG antibody; human growth hormone; hGH; selection;
KW screening; ss.
XX
OS Homo sapiens.
XX
PN WO9209690-A.
XX
PD 11-JUN-1992.
XX
PF 03-DEC-1991; 91WO-US09133.
XX
PR 03-DEC-1990; 90US-0621667.
PR 10-APR-1991; 91US-0683400.
PR 14-JUN-1991; 91US-0715300.
PR 08-AUG-1991; 91US-0743614.
XX
PA (GETH) GENENTECH INC.
XX
PI Bass S, Garrard LJ, Greene R, Henner DJ, Lowman HB;
PI Matthews DJ, Wells JA;
XX
DR WPI; 1992-217069/26.
XX
PT Selecting and enriching variant proteins - comprises fusing gene
PT encoding e.g. growth hormone to part of M13 phage coat protein
PT and mutagenising fusion prior to selection
XX
PS Claim 24; Page 75; 102pp; English.
XX
CC This sequence represents a preferred hGH variant of the invention.
CC The variants were produced by digestion of each of the one-helix
CC variants with EcoRI and BstXI. The large fragment of each helix-4b
CC variant was then isolated and ligated with the small fragment from
CC each helix-1 variant to yield a set of new variants.
CC The one helix variants were made by either random cassette mutagenesis,
CC or site directed oligonucleotide mutagenesis within helix-4 and 1
CC of hGH.
CC Some of these hGH variants have stronger affinities for the hGH
CC receptor and binding protein.
CC This sequence was not given in the specification but generated from
CC the known hGH sequence, and the modifications described in the
CC specification.
XX
SQ Sequence 191 AA;

Query Match 96.6%; Score 84; DB 13; Length 191;

```
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           ||||:||||||||||||
Db     176 ylrimqcrsvegscgf 191


RESULT  21
AAR24766
ID   AAR24766 standard; Protein; 191 AA.
XX
AC   AAR24766;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #54 - 174S 176Y 10L 14N 18S 21H 167R 171D 175T 179I.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           ||||:||||||||||||
Db     176 ylrimqcrsvegscgf 191


RESULT  22
AAR24769
ID   AAR24769 standard; Protein; 191 AA.
XX
AC   AAR24769;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #57 - 174S 176Y 10F 14S 18T 21G 167R 171D 175T 179T.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           ||||:||||||||||||
Db     176 ylrimqcrsvegscgf 191


RESULT  23
AAR24770
ID   AAR24770 standard; Protein; 191 AA.
XX
AC   AAR24770;
XX
DT   08-DEC-1992  (first entry)
XX
```

```
DE   hGH variant #58 - 174S 176Y 10A 14W 18D 21N 167R 171D 175T 179I.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT  24
AAR24776
ID   AAR24776 standard; Protein; 191 AA.
XX
AC   AAR24776;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #64 - 174S 176Y 10H 14Q 18Y 21S 167R 171D 175T 179I.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             96.6%;  Score 84;  DB 13;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 3.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          ||||:|||||||||||
Db    176 ylrimqcrsvegscgf 191


RESULT  25
AAY78432
ID   AAY78432 standard; Peptide; 25 AA.
XX
AC   AAY78432;
XX
DT   09-MAY-2000  (first entry)
XX
DE   Human growth hormone variant peptide sequence #3.
XX
KW   Human growth hormone; hGH; prolactin; placental lactogen;
KW   modification; mutagenesis.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US6013478-A.
XX
PD   11-JAN-2000.
XX
PF   24-JUN-1998;   98US-0104036.
XX
PR   26-OCT-1989;   89US-0428066.
PR   27-APR-1992;   92US-0875204.
```

PR 13-OCT-1992; 92US-0960227.
PR 02-FEB-1994; 94US-0190723.
PR 06-JUN-1995; 95US-0483039.
PR 30-JUN-1997; 97US-0903398.
PR 28-OCT-1988; 88US-0264611.
XX
PA (GETH) GENENTECH INC.
XX
PI Wells JA, Cunningham BC;
XX
DR WPI; 2000-159873/14.
XX
PT Recombinant production of variant polypeptides, e.g. growth hormone
PT variants with altered receptor specificity, using cells transformed
PT with DNA selected by scanning mutagenesis in at least one peptide
PT domain -
XX
PS Example 8; Fig 7; 83pp; English.
XX
CC The present invention describes the production of a polypeptide variant
CC (I) comprising segment substituted and residue substituted growth
CC hormone, prolactin or placental lactogens. The method is particularly
CC used to produce variants of growth hormone (GH), prolactin or placental
CC lactogen, but may also be applied to receptors, interferons, and
CC colony-stimulating factors. A particular application is the production
CC of human GH variants with altered (decreased or increased) binding
CC interaction with the somatogenic receptor, i.e. compounds useful as
CC human GH (ant)agonists and which may have higher potency for stimulating
CC other human GH receptors, and as standards or tracers in immunoassays
CC for human GH. This method of DNA selection identifies the biologically
CC active residues in active domains, including those critical for
CC interaction with different targets. The present sequence represents a
CC human GH variant peptide sequence, which is used in the exemplification
CC of the present invention.
XX
SQ Sequence 25 AA;

Query Match 95.4%; Score 83; DB 21; Length 25;
Best Local Similarity 93.8%; Pred. No. 6.8e-06;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 10 flrivqcrsvegscgf 25

RESULT 26
AAP40352
ID AAP40352 standard; Protein; 56 AA.
XX
AC AAP40352;
XX
DT 20-JUL-1992 (first entry)
XX
DE Synthetic human growth hormone.
XX
KW Growth hormone.
XX
OS Synthetic.
XX
PN JP59106297-A.
XX
PD 19-JUN-1984.
XX
PF 07-DEC-1982; 82JP-0214230.
XX
PR 07-DEC-1982; 82JP-0214230.
XX
PA (RIKA) RIKAGAKU KENKYUSHO.
XX
DR WPI; 1984-186334/30.
DR N-PSDB; AAN40263.
XX
PT Prepn. of carboxy-terminated gene of human growth hormone - by
PT solid phase condensn. of 3-ester(s) of desoxyguanosine,
PT desoxycytidine, desoxyadenosine and thymidine with dinucleoside.
XX
PS Claim 1; Page 2; 14pp; Japanese.
XX
CC The protein was produced from a synthetic gene prepd. by success-
CC ive solid phase condensation of 3'-esters of deoxyguanosine, deoxy-
CC cytidine, deoxyadenosine and thymidine with a dinucleoside, to form
CC a group of fragments, followed by enzymic 5'-phosphorylation and
CC condensation with DNA ligase. The four dNTPs are first converted to
CC the corresp. succinates, and each ester is fixed to a 1%-divinyl
CC benzene/styrene copolymer to form a solid nucleoside carrier, which
CC serves as the starting material for the synthsis of each fragment.
CC The carrier is successively condensed with dinucleotides in a
CC definite order by the action of a condensation agent such as
CC mesitylenesulphonyl-3-nitrotriazolide. Each oligonucleotide prepd.
CC in this way is then phosphorylated and coupled with DNA ligase.
XX
SQ Sequence 56 AA;

Query Match 95.4%; Score 83; DB 5; Length 56;
Best Local Similarity 93.8%; Pred. No. 1.5e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 41 flrivqcrsvegscgf 56

RESULT 27
ABB23044
ID ABB23044 standard; Protein; 65 AA.
XX
AC ABB23044;
XX
DT 23-JAN-2002 (first entry)
XX
DE Protein #5043 encoded by probe for measuring heart cell gene expression.
XX
KW Human; gene expression; heart; microarray; vascular system;
KW cardiovascular disease; hypertension; cardiac arrhythmia;
KW congenital heart disease.
XX
OS Homo sapiens.
XX
PN WO200157274-A2.
XX
PD 09-AUG-2001.
XX
PF 30-JAN-2001; 2001WO-US00666.
XX
PR 04-FEB-2000; 2000US-0180312.
PR 26-MAY-2000; 2000US-0207456.
PR 30-JUN-2000; 2000US-0608408.
PR 03-AUG-2000; 2000US-0632366.
PR 21-SEP-2000; 2000US-0234687.
PR 27-SEP-2000; 2000US-0236359.
PR 04-OCT-2000; 2000GB-0024263.
XX
PA (MOLE-) MOLECULAR DYNAMICS INC.
XX
PI Penn SG, Hanzel DK, Chen W, Rank DR;
XX
DR WPI; 2001-488899/53.
XX
PT Single exon nucleic acid probes for analyzing gene expression in human
PT hearts -
XX
PS Claim 15; SEQ ID No 24814; 530pp; English.
XX

```
CC   The present invention relates to single exon nucleic acid probes for
CC   measuring human gene expression in a sample derived from human heart (see
CC   ABA21535-ABA41305). The present sequence is a protein encoded by one such
CC   probe. The probes may be used for predicting, measuring and displaying
CC   gene expression in samples derived from the human heart via microarrays.
CC   By measuring gene expression, the probes are useful for predicting,
CC   diagnosing, grading, staging, monitoring and prognosing diseases of the
CC   human heart and vascular system e.g. cardiovascular disease,
CC   hypertension, cardiac arrhythmias and congenital heart disease.
CC   Note: The sequence data for this patent did not form part of the printed
CC   specification, but was obtained in electronic format directly from WIPO
CC   at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ   Sequence   65 AA;


  Query Match             95.4%;  Score 83;  DB 22;  Length 65;
  Best Local Similarity   93.8%;  Pred. No. 1.7e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||||
Db     50 flrivqcrsvegscgf 65


RESULT  28
AAM31150
ID   AAM31150 standard; Protein; 65 AA.
XX
AC   AAM31150;
XX
DT   17-OCT-2001  (first entry)
XX
DE   Peptide #5187 encoded by probe for measuring placental gene expression.
XX
KW   Probe; microarray; human; placenta; antenatal diagnosis;
KW   genetic disorder.
XX
OS   Homo sapiens.
XX
PN   WO200157272-A2.
XX
PD   09-AUG-2001.
XX
PF   30-JAN-2001; 2001WO-US00663.
XX
PR   04-FEB-2000; 2000US-0180312.
PR   26-MAY-2000; 2000US-0207456.
PR   30-JUN-2000; 2000US-0608408.
PR   03-AUG-2000; 2000US-0632366.
PR   21-SEP-2000; 2000US-0234687.
PR   27-SEP-2000; 2000US-0236359.
PR   04-OCT-2000; 2000GB-0024263.
XX
PA   (MOLE-) MOLECULAR DYNAMICS INC.
XX
PI   Penn SG,  Hanzel DK,  Chen W,  Rank DR;
XX
DR   WPI; 2001-488897/53.
XX
PT   Human genome-derived single exon nucleic acid probes useful for
PT   analyzing gene expression in human placenta -
XX
PS   Claim 27; SEQ ID No 31419; 654pp; English.
XX
CC   The present invention relates to single exon nucleic acid probes (SENP:
CC   see AAI31315-AAI57546). The present sequence is a peptide encoded by one
CC   such probe. The probes are useful for producing a microarray for
CC   predicting, measuring and displaying gene expression in samples derived
CC   from human placenta. The probes are useful for antenatal diagnosis of
CC   human genetic disorders.
XX
SQ   Sequence   65 AA;


  Query Match             95.4%;  Score 83;  DB 22;  Length 65;
  Best Local Similarity   93.8%;  Pred. No. 1.7e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||||
Db     50 flrivqcrsvegscgf 65


RESULT  29
AAW26202
ID   AAW26202 standard; protein; 176 AA.
XX
AC   AAW26202;
XX
DT   29-JAN-1998  (first entry)
XX
DE   20 kDa human growth hormone (hGH) example 1.
XX
KW   Human growth hormone; hGH; pituitary dwarfism; creatinine;
KW   solubility; preparation.
XX
OS   Homo sapiens.
XX
PN   EP787497-A2.
XX
PD   06-AUG-1997.
XX
PF   30-JAN-1997;   97EP-0300607.
XX
PR   02-FEB-1996;   96JP-0017342.
XX
PA   (MITK ) MITSUI TOATSU CHEM INC.
XX
PI   Aoki M,  Fukuhara A,  Ito T,  Kobayashi H,  Kusuhara N;
PI   Miyama Y,  Sato T,  Uchida H;
XX
DR   WPI; 1997-387281/36.
XX
PT   Human growth hormone of molecular weight 20000 - stabilised and
PT   solubilised by addition of a water-soluble heterocyclic compound,
PT   for use in pituitary dwarfism therapy
XX
PS   Disclosure; Page 5; 15pp; English.
XX
CC   This peptide is an example of the 20 kDa human growth hormone (hGH).
CC   There are 2 known types of hGH, a 22 kDa hGH and a 20 kDa hGH. Although
CC   the 22 kDa hGH is produced by means of recombinant DNA technology and
CC   used to treat pituitary dwarfism, the 20 kDa hGH has never been produced
CC   on an industrial scale, and has never been used for medical treatment.
CC   The 20 kDa hGH has a very low solubility in water, which may be due to
CC   hydrophobic interaction of protein molecules. A novel pharmaceutical
CC   preparation has been formulated, comprising a 20 kDa hGH (or a derivative
CC   of it) and a water-soluble heterocyclic compound (e.g. creatinine), which
CC   improves the solubility and stability of the hGH. The pharmaceutical
CC   preparations are suitable for injection. The 20 kD hGH can be
CC   administered with the 22 kDa hGH in the course of pituitary dwarfism
CC   treatment.
XX
SQ   Sequence   176 AA;


  Query Match             95.4%;  Score 83;  DB 18;  Length 176;
  Best Local Similarity   93.8%;  Pred. No. 4.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||||
Db    161 flrivqcrsvegscgf 176
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```
RESULT  30
AAW26203
ID   AAW26203 standard; peptide; 176 AA.
XX
AC   AAW26203;
XX
DT   29-JAN-1998  (first entry)
XX
DE   20 kDa human growth hormone (hGH) example 2.
XX
KW   Human growth hormone; hGH; pituitary dwarfism; creatinine;
KW   solubility; preparation.
XX
OS   Homo sapiens.
XX
PN   EP787497-A2.
XX
PD   06-AUG-1997.
XX
PF   30-JAN-1997;   97EP-0300607.
XX
PR   02-FEB-1996;   96JP-0017342.
XX
PA   (MITK ) MITSUI TOATSU CHEM INC.
XX
PI   Aoki M,  Fukuhara A,  Ito T,  Kobayashi H,  Kusuhara N;
PI   Miyama Y,  Sato T,  Uchida H;
XX
DR   WPI; 1997-387281/36.
XX
PT   Human growth hormone of molecular weight 20000 - stabilised and
PT   solubilised by addition of a water-soluble heterocyclic compound,
PT   for use in pituitary dwarfism therapy
XX
PS   Disclosure; Page 6; 15pp; English.
XX
CC   This peptide is an example of the 20 kDa human growth hormone (hGH).
CC   There are 2 known types of hGH, a 22 kDA hGH and a 20 kDa hGH. Although
CC   the 22 kDa hGH is produced by means of recombinant DNA technology and
CC   used to treat pituitary dwarfism, the 20 kDa hGH has never been produced
CC   on an industrial scale, and has never been used for medical treatment.
CC   The 20 kDa hGH has a very low solubility in water, which may be due to
CC   hydrophobic interaction of protein molecules. A novel pharmaceutical
CC   preparation has been formulated, comprising a 20 kDa hGH (or a derivative
CC   of it) and a water-soluble heterocyclic compound (e.g. creatinine), which
CC   improves the solubility and stability of the hGH. The pharmaceutical
CC   preparations are suitable for injection. The 20 kD hGH can be
CC   administered with the 22 kDa hGH in the course of pituitary dwarfism
CC   treatment.
XX
SQ   Sequence   176 AA;


  Query Match            95.4%;  Score 83;  DB 18;  Length 176;
  Best Local Similarity   93.8%;  Pred. No. 4.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||
Db    161 flrivqcrsvegscgf 176


RESULT  31
AAW23662
ID   AAW23662 standard; protein; 176 AA.
XX
AC   AAW23662;
XX
DT   13-OCT-1997  (first entry)
XX
DE   Authentic 20-kilodalton human growth hormone protein.
XX
KW   20kD hGH; human; medicinal; hormone replacement therapy; lipolysis;
KW   serum IGF-1 level.
XX
OS   Homo sapiens.
XX
PN   EP753307-A2.
XX
PD   15-JAN-1997.
XX
PF   01-JUL-1996;   96EP-0304855.
XX
PR   05-DEC-1995;   95JP-0316883.
PR   29-JUN-1995;   95JP-0163572.
PR   29-JUN-1995;   95JP-0163275.
XX
PA   (MITK ) MITSUI TOATSU CHEM INC.
XX
PI   Asada N,  Honjo M,  Horikomi K,  Ikeda M,  Kamioka T;
XX
DR   WPI; 1997-079182/08.
XX
PT   Medicaments contg. 20 kD human growth hormone - useful for hormone
PT   replacement therapy and to stimulate lipolysis e.g. for improving
PT   body compsn.
XX
PS   Claim 2; Page 12; 19pp; English.
XX
CC   The present sequence represents an authentic 20-kilodalton human
CC   growth hormone (20kD hGH) protein. The 20kD hGH is used in medicinal
CC   compositions as an effective component and a pharmaceutically
CC   acceptable carrier or dilutent. The protein can be used for growth
CC   hormone replacement therapy in adults, especially hGH-deficient adults,
CC   to improve body composition, stimulate lipolysis and/or increase serum
CC   IGF-1 levels. The 20 kD hGH has less tendency to induce glucose
CC   intolerance than the known 22 kD hGH.
XX
SQ   Sequence   176 AA;


  Query Match            95.4%;  Score 83;  DB 18;  Length 176;
  Best Local Similarity   93.8%;  Pred. No. 4.4e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||
Db    161 flrivqcrsvegscgf 176


RESULT  32
AAW23661
ID   AAW23661 standard; protein; 176 AA.
XX
AC   AAW23661;
XX
DT   13-OCT-1997  (first entry)
XX
DE   Authentic 20-kilodalton human growth hormone protein.
XX
KW   20kD hGH; human; medicinal; hormone replacement therapy; lipolysis;
KW   serum IGF-1 level.
XX
OS   Homo sapiens.
XX
PN   EP753307-A2.
XX
PD   15-JAN-1997.
XX
PF   01-JUL-1996;   96EP-0304855.
XX
PR   05-DEC-1995;   95JP-0316883.
PR   29-JUN-1995;   95JP-0163572.
PR   29-JUN-1995;   95JP-0163275.
XX
PA   (MITK ) MITSUI TOATSU CHEM INC.
```

XX
PI Asada N, Honjo M, Horikomi K, Ikeda M, Kamioka T;
XX
DR WPI; 1997-079182/08.
XX
PT Medicaments contg. 20 kD human growth hormone - useful for hormone
PT replacement therapy and to stimulate lipolysis e.g. for improving
PT body compsn.
XX
PS Claim 2; Page 11; 19pp; English.
XX
CC The present sequence represents an authentic 20-kilodalton human
CC growth hormone (20kD hGH) protein. The 20kD hGH is used in medicinal
CC compositions as an effective component and a pharmaceutically
CC acceptable carrier or dilutent. The protein can be used for growth
CC hormone replacement therapy in adults, especially hGH-deficient adults,
CC to improve body composition, stimulate lipolysis and/or increase serum
CC IGF-1 levels. The 20 kD hGH has less tendency to induce glucose
CC intolerance than the known 22 kD hGH.
XX
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 18; Length 176;
Best Local Similarity 93.8%; Pred. No. 4.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 161 flrivqcrsvegscgf 176

RESULT 33
AAW59762
ID AAW59762 standard; protein; 176 AA.
XX
AC AAW59762;
XX
DT 12-OCT-1998 (first entry)
XX
DE Amino acid sequence of clone 2 of the human growth hormone.
XX
KW Human; growth hormone; inhibition; tumour.
XX
OS Homo sapiens.
XX
PN JP10182699-A.
XX
PD 07-JUL-1998.
XX
PF 26-DEC-1996; 96JP-0347433.
XX
PR 26-DEC-1996; 96JP-0347433.
XX
PA (MITC) MITSUI PETROCHEM IND CO LTD.
XX
DR WPI; 1998-433892/37.
XX
PT Human growth hormone agent - useful in preparation of therapeutics
PT for inhibiting growth of tumours
XX
PS Claim 2; Page 5; 6pp; Japanese.
XX
CC This is the amino acid sequence of the human growth hormone used in the
CC method of the invention involving the preparation of therapeutics for
CC inhibiting tumour growth.
XX
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 19; Length 176;
Best Local Similarity 93.8%; Pred. No. 4.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 161 flrivqcrsvegscgf 176

RESULT 34
AAW59761
ID AAW59761 standard; protein; 176 AA.
XX
AC AAW59761;
XX
DT 12-OCT-1998 (first entry)
XX
DE Amino acid sequence of clone 1 of the human growth hormone.
XX
KW Human; growth hormone; inhibition; tumour.
XX
OS Homo sapiens.
XX
PN JP10182699-A.
XX
PD 07-JUL-1998.
XX
PF 26-DEC-1996; 96JP-0347433.
XX
PR 26-DEC-1996; 96JP-0347433.
XX
PA (MITC) MITSUI PETROCHEM IND CO LTD.
XX
DR WPI; 1998-433892/37.
XX
PT Human growth hormone agent - useful in preparation of therapeutics
PT for inhibiting growth of tumours
XX
PS Claim 2; Pages 4-5; 6pp; Japanese.
XX
CC This is the amino acid sequence of the human growth hormone used in the
CC method of the invention involving the preparation of therapeutics for
CC inhibiting tumour growth.
XX
SQ Sequence 176 AA;

Query Match 95.4%; Score 83; DB 19; Length 176;
Best Local Similarity 93.8%; Pred. No. 4.4e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 161 flrivqcrsvegscgf 176

RESULT 35
AAR76820
ID AAR76820 standard; Protein; 177 AA.
XX
AC AAR76820;
XX
DT 07-DEC-1995 (first entry)
XX
DE hGHV-3(53) growth hormone splice variant.
XX
KW Growth hormone; somatotropin; splice variant; hyperpituitism;
KW hGHV-3(53); gene therapy.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Peptide 1..26
FT /label= Sig_peptide
XX
PN WO9520398-A.

```
XX
PD   03-AUG-1995.
XX
PF   27-JAN-1995;   95WO-US01130.
XX
PR   27-JAN-1994;   94US-0187756.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Adams MD,  Coleman TA,  Gocayne JD,  Rosen CA;
XX
DR   WPI; 1995-275295/36.
DR   N-PSDB; AAQ93150.
XX
PT   DNA and protein sequences of new splice variants of human growth
PT   hormone - useful for diagnosis and treatment of conditions associated
PT   with abnormal production of growth hormone, eg. Turner's syndrome,
PT   gigantism and acromegaly.
XX
PS   Claim 21; Page 35-36; 53pp; English.
XX
CC   The hGHV-3(53) cDNA sequence given in AAQ93150 is generated by
CC   alternative splicing of wild-type hGH pre-mRNA in which the splice donor
CC   site of exon-2 is fused to exon-3, resulting in removal of 120
CC   nucleotides. HGHV-3(53) is partic. useful for treatment of
CC   hyperpituitism.
XX
SQ   Sequence   177 AA;


  Query Match             95.4%;  Score 83;  DB 16;  Length 177;
  Best Local Similarity   93.8%;  Pred. No. 4.5e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           :||||||||||||||||
Db     162 flrivqcrsvegscgf 177


RESULT  36
AAY84644
ID   AAY84644 standard; Protein; 190 AA.
XX
AC   AAY84644;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of des-Phe human growth hormone (hGH).
XX
KW   Human growth hormone; hGH; idiopathic short stature; Turner's syndrome;
KW   chronic renal failure; Somatotropin Deficiency Syndrome; cachexia;
KW   adult growth hormone deficiency; acquired immunodeficiency syndrome;
KW   AIDS.
XX
OS   Homo sapiens.
XX
PN   WO200015664-A1.
XX
PD   23-MAR-2000.
XX
PF   10-SEP-1999;   99WO-AU00742.
XX
PR   10-SEP-1998;   98AU-0005821.
XX
PA   (BRES-) BRESAGEN LTD.
XX
PI   Bastiras S,  Robins A;
XX
DR   WPI; 2000-271384/23.
DR   N-PSDB; AAA12724.
XX
PT   des-Phe human growth hormones useful for treating e.g. Somatotropin
PT   Deficiency Syndrome and cachexia in acquired immunodeficiency syndrome
PT   (AIDS) -
XX
PS   Disclosure; Page 15-16; 18pp; English.
XX
CC   The present sequence represents a des-Phe human growth hormone (hGH).
CC   des-Phe hGH is identical to natural hGH, however the first amino acid
CC   (phenylalanine) is absent. hGH is a single chain unglycosylated
CC   protein. des-Phe hGH can be used to treat a range of diseases associated
CC   with decreased hGH expression in a patient. These include idiopathic
CC   short stature, Turner's syndrome, chronic renal failure, Somatotropin
CC   Deficiency Syndrome (adult growth hormone deficiency) and cachexia in
CC   acquired immunodeficiency syndrome (AIDS).
XX
SQ   Sequence   190 AA;


  Query Match             95.4%;  Score 83;  DB 21;  Length 190;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           :||||||||||||||||
Db     175 flrivqcrsvegscgf 190


RESULT  37
AAP60016
ID   AAP60016 standard; Protein; 191 AA.
XX
AC   AAP60016;
XX
DT   31-JUL-1991  (first entry)
XX
DE   Sequence of human growth hormone (BGH).
XX
KW   Somatotropin; somatotrophin.
XX
OS   Homo sapiens.
XX
PN   EP192629-A.
XX
PD   27-AUG-1986.
XX
PF   21-FEB-1986;   86EP-0870023.
XX
PR   22-FEB-1985;   85US-0704677.
PR   22-FEB-1985;   85US-0704341.
PR   25-AUG-1986;   86US-0900017.
XX
PA   (MONS ) MONSANTO CO.
XX
PI   Bentle LA,  Mitchell JW,  Storrs SB,  Shimamoto GT;
XX
DR   WPI; 1986-227173/35.
XX
PT   Solubilisation and naturation of heterologous somatotropin - by
PT   treating refractory bodies with urea or di:methyl-sulphone then
PT   oxidising
XX
PS   Disclosure; Page 4; 13pp; English.
XX
CC   The patentors claim a method for solubilisation and naturation of
CC   somatotropin protein from refractile bodies (RB) of a host cell. The
CC   method is used for naturation of heterologous bovine or porcine
CC   somatotropins (claimed), partic. expressed by E. coli, giving
CC   biologically active material.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 7;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||||
Db    176 flrivqcrsvegscgf 191


RESULT  38
AAR24754
ID   AAR24754 standard; Protein; 191 AA.
XX
AC   AAR24754;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #42 - 174S 176Y 10F 14L 18S 21S 167K 171N 175T 179V.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 13;  Length 191;
  Best Local Similarity   87.5%;  Pred. No. 4.8e-05;
  Matches   14;  Conservative    2;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          |||::||||||||||||
Db    176 ylrvmqcrsvegscgf 191


RESULT  39
AAR24772
ID   AAR24772 standard; Protein; 191 AA.
XX
AC   AAR24772;
XX
DT   08-DEC-1992  (first entry)
XX
DE   hGH variant #60 - 174S 176Y 10F 14S 18L 21A 167N 171S 175T 179V.
XX
KW   humanised IgG antibody; human growth hormone; hGH; selection;
KW   screening; ss.
XX
OS   Homo sapiens.
XX
PN   WO9209690-A.
XX
PD   11-JUN-1992.
XX
PF   03-DEC-1991;   91WO-US09133.
XX
PR   03-DEC-1990;   90US-0621667.
PR   10-APR-1991;   91US-0683400.
PR   14-JUN-1991;   91US-0715300.
PR   08-AUG-1991;   91US-0743614.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Bass S,  Garrard LJ,  Greene R,  Henner DJ,  Lowman HB;
PI   Matthews DJ,  Wells JA;
XX
DR   WPI; 1992-217069/26.
XX
PT   Selecting and enriching variant proteins - comprises fusing gene
PT   encoding e.g. growth hormone to part of M13 phage coat protein
PT   and mutagenising fusion prior to selection
XX
PS   Claim 24; Page 75; 102pp; English.
XX
CC   This sequence represents a preferred hGH variant of the invention.
CC   The variants were produced by digestion of each of the one-helix
CC   variants with EcoRI and BstXI. The large fragment of each helix-4b
CC   variant was then isolated and ligated with the small fragment from
CC   each helix-1 variant to yield a set of new variants.
CC   The one helix variants were made by either random cassette mutagenesis,
CC   or site directed oligonucleotide mutagenesis within helix-4 and 1
CC   of hGH.
CC   Some of these hGH variants have stronger affinities for the hGH
CC   receptor and binding protein.
CC   This sequence was not given in the specification but generated from
CC   the known hGH sequence, and the modifications described in the
CC   specification.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 13;  Length 191;
  Best Local Similarity   87.5%;  Pred. No. 4.8e-05;
  Matches   14;  Conservative    2;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          |||::||||||||||||
Db    176 ylrvmqcrsvegscgf 191


RESULT  40
AAW38221
ID   AAW38221 standard; Protein; 191 AA.
XX
AC   AAW38221;
XX
DT   19-MAR-1998  (first entry)
XX
DE   Human growth hormone mutant Cys53Ala/Arg77Cys.
XX
```

```
KW   Mutant; human growth hormone; hGH; treatment; gigantism;
KW   acromegaly; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 53
FT                   /note= "wild type Cys replaced by Ala"
FT   Misc-difference 77
FT                   /note= "wild type Arg replaced by Cys"
XX
PN   EP790305-A1.
XX
PD   20-AUG-1997.
XX
PF   12-FEB-1997;   97EP-0300902.
XX
PR   18-JUN-1996;   96JP-0178643.
PR   13-FEB-1996;   96JP-0050940.
XX
PA   (JCRP-) JCR PHARM CO LTD.
XX
PI   Chihara K;
XX
DR   WPI; 1997-404732/38.
DR   N-PSDB; AAT95815.
XX
PT   Mutant human growth hormone proteins - with increased receptor
PT   affinity and reduced hormone activity
XX
PS   Claim 2; Page 17; 28pp; English.
XX
CC   The present sequence is a mutant human growth hormone (hGH),
CC   which can be used to treat gigantism or acromegaly, while its DNA
CC   can be used for gene therapy. The mutant has a higher affinity for
CC   hGH receptor than wild-type hGH, can inhibit binding of hGH to
CC   its receptor and has a lower activity than wild-type hGH.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 18;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||
Db    176 flrivqcrsvegscgf 191


RESULT  41
AAW38222
ID   AAW38222 standard; Protein; 191 AA.
XX
AC   AAW38222;
XX
DT   19-MAR-1998  (first entry)
XX
DE   Human growth hormone mutant Arg77Cys/Cys165Ala.
XX
KW   Mutant; human growth hormone; hGH; treatment; gigantism;
KW   acromegaly; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 77
FT                   /note= "wild type Arg replaced by Cys"
FT   Misc-difference 165
FT                   /note= "wild type Cys replaced by Ala"
XX
PN   EP790305-A1.
XX
PD   20-AUG-1997.
XX
PF   12-FEB-1997;   97EP-0300902.
XX
PR   18-JUN-1996;   96JP-0178643.
PR   13-FEB-1996;   96JP-0050940.
XX
PA   (JCRP-) JCR PHARM CO LTD.
XX
PI   Chihara K;
XX
DR   WPI; 1997-404732/38.
DR   N-PSDB; AAT95816.
XX
PT   Mutant human growth hormone proteins - with increased receptor
PT   affinity and reduced hormone activity
XX
PS   Claim 3; Page 18; 28pp; English.
XX
CC   The present sequence encodes a mutant human growth hormone (hGH),
CC   which can be used to treat gigantism or acromegaly, while its DNA
CC   can be used for gene therapy. The mutant has a higher affinity for
CC   hGH receptor than wild-type hGH, can inhibit binding of hGH to
CC   its receptor and has a lower activity than wild-type hGH.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 18;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 YLRIVQCRSVEGSCGF 16
          :||||||||||||||
Db    176 flrivqcrsvegscgf 191


RESULT  42
AAW38220
ID   AAW38220 standard; Protein; 191 AA.
XX
AC   AAW38220;
XX
DT   19-MAR-1998  (first entry)
XX
DE   Human growth hormone mutant Arg77Cys.
XX
KW   Mutant; human growth hormone; hGH; treatment; gigantism;
KW   acromegaly; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 77
FT                   /note= "wild type Arg replaced by Cys"
XX
PN   EP790305-A1.
XX
PD   20-AUG-1997.
XX
PF   12-FEB-1997;   97EP-0300902.
XX
PR   18-JUN-1996;   96JP-0178643.
PR   13-FEB-1996;   96JP-0050940.
XX
PA   (JCRP-) JCR PHARM CO LTD.
XX
PI   Chihara K;
XX
DR   WPI; 1997-404732/38.
DR   N-PSDB; AAT95814.
XX
PT   Mutant human growth hormone proteins - with increased receptor
```

```
PT   affinity and reduced hormone activity
XX
PS   Claim 1; Page 16; 28pp; English.
XX
CC   The present sequence is a mutant human growth hormone (hGH),
CC   which can be used to treat gigantism or acromegaly, while its DNA
CC   can be used for gene therapy. The mutant has a higher affinity for
CC   hGH receptor than wild-type hGH, can inhibit binding of hGH to
CC   its receptor and has a lower activity than wild-type hGH.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 18;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           :||||||||||||||||
Db     176 flrivqcrsvegscgf 191


RESULT  43
AAW71289
ID   AAW71289 standard; protein; 191 AA.
XX
AC   AAW71289;
XX
DT   25-NOV-1998  (first entry)
XX
DE   Human growth hormone amino acid sequence.
XX
KW   Human; growth hormone; treatment; pituitary dwarfism; bone fracture;
KW   burn.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  53..165
FT   Disulfide-bond  182..189
XX
PN   JP10234386-A.
XX
PD   08-SEP-1998.
XX
PF   25-DEC-1997;   97JP-0356884.
XX
PR   26-DEC-1996;   96JP-0348033.
XX
PA   (TAKE ) TAKEDA CHEM IND LTD.
XX
DR   WPI; 1998-535038/46.
XX
PT   Method for correct folding of growth hormone - useful for treatment
PT   of dwarfism, bone fracture and burns
XX
PS   Disclosure; Fig 1; 29pp; Japanese.
XX
CC   The present sequence represents a human growth hormone. The specification
CC   describes a method for the preparation of an active type growth hormone.
CC   The method comprises obtaining a growth hormone expressed in a
CC   prokaryotic cell host by genetic engineering, and having it refolded in
CC   a redox buffer. The method is useful for obtaining correctly biologically
CC   functioning growth hormone. The active type growth hormone can be
CC   used for the treatment of pituitary dwarfism, bone fracture and burns.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 19;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           :||||||||||||||||
Db     176 flrivqcrsvegscgf 191


RESULT  44
AAY15809
ID   AAY15809 standard; protein; 191 AA.
XX
AC   AAY15809;
XX
DT   28-JUL-1999  (first entry)
XX
DE   Primary amino acid sequence of native human growth hormone.
XX
KW   Detection; fluoresce; illegal misuse; growth substance; athlete;
KW   domesticated farm animal; cattle; human growth hormone.
XX
OS   Homo sapiens.
XX
PN   WO9926069-A1.
XX
PD   27-MAY-1999.
XX
PF   16-NOV-1998;   98WO-GB03449.
XX
PR   14-NOV-1997;   97GB-0023955.
XX
PA   (GENE-) GENERIC BIOLOGICALS LTD.
XX
PI   Atkinson A,  Murphy JP;
XX
DR   WPI; 1999-338072/28.
XX
PT   Use of tagged exogenous polypeptide
XX
PS   Disclosure; Fig 1; 38pp; English.
XX
CC   The specification describes a method of detecting an exogenously
CC   administered substance from a naturally-occurring endogenous substance,
CC   the exogenous substance being tagged so that it fluoresces differently
CC   from the endogenous one at a suitable wavelength. The tagging may
CC   consist of one or more substitutions in tagged growth hormone
CC   selected from G40Y, F52Y, W86F, Y, L, I or V F103Y or I137Y;
CC   The method is used to distinguish between exogenously administered
CC   substances as compared to naturally-occurring endogenous substances.
CC   Especially mentioned is the illegal misuse of growth substances by
CC   athletes or in domesticated farm animals e.g. cattle. The present
CC   sequence represents native human growth hormone which may be used
CC   in the method of the invention.
XX
SQ   Sequence   191 AA;


  Query Match             95.4%;  Score 83;  DB 20;  Length 191;
  Best Local Similarity   93.8%;  Pred. No. 4.8e-05;
  Matches   15;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 YLRIVQCRSVEGSCGF 16
           :||||||||||||||||
Db     176 flrivqcrsvegscgf 191


RESULT  45
AAY15810
ID   AAY15810 standard; Protein; 191 AA.
XX
AC   AAY15810;
XX
DT   28-JUL-1999  (first entry)
XX
DE   Tagged human growth hormone.
XX
```

KW Detection; fluoresce; illegal misuse; growth substance; athlete;
KW domesticated farm animal; cattle; human growth hormone.
XX
OS Synthetic.
OS Homo sapiens.
XX
PN WO9926069-A1.
XX
PD 27-MAY-1999.
XX
PF 16-NOV-1998; 98WO-GB03449.
XX
PR 14-NOV-1997; 97GB-0023955.
XX
PA (GENE-) GENERIC BIOLOGICALS LTD.
XX
PI Atkinson A, Murphy JP;
XX
DR WPI; 1999-338072/28.
DR N-PSDB; AAX59843.
XX
PT Use of tagged exogenous polypeptide
XX
PS Example 2; Fig 3; 38pp; English.
XX
CC The specification describes a method of detecting an exogenously
CC administered substance from a naturally-occurring endogenous substance,
CC the exogenous substance being tagged so that it fluoresces differently
CC from the endogenous one at a suitable wavelength. The tagging may
CC consist of one or more substitutions in tagged growth hormone
CC selected from G40Y, F52Y, W86F, Y, L, I or V F103Y or I137Y;
CC The method is used to distinguish between exogenously administered
CC substances as compared to naturally-occurring endogenous substances.
CC Especially mentioned is the illegal misuse of growth substances by
CC athletes or in domesticated farm animals e.g. cattle. The present
CC sequence represents a tagged human growth hormone, which may be used
CC in the method of the invention.
XX
SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 20; Length 191;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 176 flrivqcrsvegscgf 191

RESULT 46
AAY04396
ID AAY04396 standard; protein; 191 AA.
XX
AC AAY04396;
XX
DT 29-JUN-1999 (first entry)
XX
DE Natural human 22kDa growth hormone.
XX
KW Human; 22kDa growth hormone; hGH; mutant; thrombin; resistance;
KW plasmin; decomposition.
XX
OS Homo sapiens.
XX
PN JP11092499-A.
XX
PD 06-APR-1999.
XX
PF 22-SEP-1997; 97JP-0275277.
XX
PR 22-SEP-1997; 97JP-0275277.
XX
PA (SUMU) SUMITOMO SEIYAKU KK.
XX
DR WPI; 1999-283567/24.
XX
PT A human growth hormone mutant - with equivalent activity to natural
PT human growth hormone
XX
PS Example 1; Page 5-6; 10pp; Japanese.
XX
CC The present invention describes a human growth hormone mutant in which
CC the 134th Arg and the 135th Thr are replaced respectively by Asp and Pro
CC in the 1st to the 191st amino acid sequence of natural type human 22 kDa
CC growth hormone (hGH) and which has a resistance against decomposition by
CC thrombin. The present sequence represents the natural hGH. Also
CC described are: (1) a hGH mutant in which the 134th Arg, the 135th Thr
CC and the 140th Lys are replaced respectively by Asp, Pro and Ala in the
CC amino acid sequence of natural type hGH and which has a resistance
CC against decomposition by thrombin and plasmin; and (2) a drug
CC preparation containing the above hGH mutant as the active component.
CC The mutant hGH shows an activity approximately equivalent to that of
CC natural type hGH and shows a high stability in blood and body fluid.
XX
SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 20; Length 191;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 176 flrivqcrsvegscgf 191

RESULT 47
AAY04397
ID AAY04397 standard; protein; 191 AA.
XX
AC AAY04397;
XX
DT 29-JUN-1999 (first entry)
XX
DE Mutant human 22kDa growth hormone.
XX
KW Human; 22kDa growth hormone; hGH; mutant; thrombin; resistance;
KW plasmin; decomposition.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN JP11092499-A.
XX
PD 06-APR-1999.
XX
PF 22-SEP-1997; 97JP-0275277.
XX
PR 22-SEP-1997; 97JP-0275277.
XX
PA (SUMU) SUMITOMO SEIYAKU KK.
XX
DR WPI; 1999-283567/24.
XX
PT A human growth hormone mutant - with equivalent activity to natural
PT human growth hormone
XX
PS Claim 1; Page 6-7; 10pp; Japanese.
XX
CC The present invention describes a human growth hormone mutant in which
CC the 134th Arg and the 135th Thr are replaced respectively by Asp and Pro
CC in the 1st to the 191st amino acid sequence of natural type human 22 kDa
CC growth hormone (hGH) and which has a resistance against decomposition by
CC thrombin. The present sequence represents the mutant hGH. Also
CC described are: (1) a hGH mutant in which the 134th Arg, the 135th Thr

CC and the 140th Lys are replaced respectively by Asp, Pro and Ala in the
CC amino acid sequence of natural type hGH and which has a resistance
CC against decomposition by thrombin and plasmin; and (2) a drug
CC preparation containing the above hGH mutant as the active component.
CC The mutant hGH shows an activity approximately equivalent to that of
CC natural type hGH and shows a high stability in blood and body fluid.
XX
SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 20; Length 191;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 176 flrivqcrsvegscgf 191

RESULT 48
AAB19836
ID AAB19836 standard; Protein; 191 AA.
XX
AC AAB19836;
XX
DT 05-MAR-2001 (first entry)
XX
DE Human growth hormone.
XX
KW Human growth hormone; somatotropin; hGH; aminopeptidase;
KW Aeromonas proteolytica; recombinant protein.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 53..165
FT Disulfide-bond 182..189
XX
PN WO200066761-A2.
XX
PD 09-NOV-2000.
XX
PF 26-APR-2000; 2000WO-US08746.
XX
PR 30-APR-1999; 99US-0132062.
XX
PA (MONS) MONSANTO CO.
XX
PI Tou JS, Taylor DW;
XX
DR WPI; 2001-015984/02.
XX
PT Removing N-terminal alanyl group from recombinant protein such as human
PT growth hormone to yield proteins having their native sequences,
PT involves contacting protein with Aeromonas aminopeptidase -
XX
PS Example 1; Page 24; 48pp; English.
XX
CC The present sequence is that of native human growth hormone (hGH).
CC This form of the hormone can be obtained from recombinant hGH
CC having an N-terminal alanine residue (see AAB19835) by in vitro
CC cleavage using an aminopeptides from the marine bacterium
CC Aeromonas proteolytica. This represents an example of the use of
CC this enzyme to remove N-terminal Ala residues from polypeptides,
CC especially recombinant proteins, to yield proteins having their
CC native amino acid sequences. An efficient method for converting
CC Ala-hGH to hGH involves expression of Ala-hGH in E. coli, recovery
CC of inclusion bodies, solubilization and refolding in detergent,
CC detergent removal by ultrafiltration, selective precipitation,
CC enzyme cleavage and 2 column chromatography steps. The
CC aminopeptidase can be used in soluble form or immobilized to a
CC solid support, for reactions carried out in vitro.
XX
SQ Sequence 191 AA;

Query Match 95.4%; Score 83; DB 22; Length 191;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 176 flrivqcrsvegscgf 191

RESULT 49
AAP90129
ID AAP90129 standard; protein; 192 AA.
XX
AC AAP90129;
XX
DT 06-FEB-1996 (revised)
DT 01-NOV-1989 (first entry)
XX
DE Human growth hormone.
XX
KW Human growth hormone; fusion protein; recombinant
KW vector.
XX
OS Homo sapiens (Human).
XX
PN JP01144981-A.
XX
PD 07-JUN-1989.
XX
PF 02-DEC-1987; 87JP-0304937.
XX
PR 02-DEC-1987; 87JP-0304937.
XX
PA (WAKU) WAKUNGA SEIYAKU KK.
XX
DR WPI; 1989-209284/29.
DR N-PSDB; AAN90269.
XX
PT Recombinant vector contg. fusion protein - consisting of human
PT growth hormone or deriv. ligated to foreign protein, for stability
PT and high yield.
XX
PS Disclosure; Fig 1; 19pp; Japanese.
XX
CC The invention consists of a vector contg. a fusion protein which is
CC formed by ligating, downstream of a promoter, hGH or a deriv. (pref.
CC formed by subtstn. of Met-14 with Leu) and a foreign protein.
CC Stability of the vector in the host is greatly increased so the
CC protein yield is higher.
XX
SQ Sequence 192 AA;

Query Match 95.4%; Score 83; DB 10; Length 192;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
:|||||||||||||||
Db 177 flrivqcrsvegscgf 192

RESULT 50
AAW92266
ID AAW92266 standard; Protein; 192 AA.
XX
AC AAW92266;
XX
DT 08-JUN-1999 (first entry)
XX

DE Human anti-angiogenic peptide hGH-V Met-1Phe191.
XX
KW Human; anti-angiogenic; prolactin; placental lactogen; hPL; angiogenesis;
KW growth hormone; hGH; hGH-V; capillary endothelial cell proliferation;
KW placental vascularisation; pregnancy; treatment; angiogenic disease;
KW tumour; inhibitor; malignant; angiofibroma; arteriovenous malformation;
KW arthritis; atherosclerotic plaques; corneal graft neovascularisation;
KW wound healing; proliferative retinopathy; macular degeneration; trachoma;
KW granulation; glaucoma; ocular; uveitis; fracture; Osler-Weber syndrome;
KW psoriasis; fibroplasia; scleroderma; Kaposi's sarcoma; vascular adhesion;
KW ulcer; leukaemia; reproductive disorder; contraceptive agent;
KW gene therapy; pre-eclampsia; intrauterine growth retardation;
KW placental dysfunction.
XX
OS Homo sapiens.
XX
PN WO9851323-A1.
XX
PD 19-NOV-1998.
XX
PF 12-MAY-1998; 98WO-US09691.
XX
PR 13-MAY-1997; 97US-0046394.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Martial JA, Struman I, Taylor R, Weiner RI;
XX
DR WPI; 1999-045192/04.
DR N-PSDB; AAX01710.
XX
PT New anti-angiogenic peptides - comprise N-terminal fragments of
PT human placental lactogen, human growth hormone, growth hormone
PT variant or human prolactin
XX
PS Example 3; Page 51-52; 87pp; English.
XX
CC This invention describes novel human anti-angiogenic peptides derived
CC from 10 to 150 consecutive amino acids selected from the N-terminal end
CC of human placental lactogen (hPL), human growth hormone (hGH), growth
CC hormone variant (hGH-V), or human prolactin. Such peptides (i) inhibit
CC capillary endothelial cell proliferation and organisation (ii) inhibit
CC angiogenesis in chick chorioallantoic membrane and (iii) binds to at
CC least one specific receptor which does not bind an intact full length
CC hGH, hPL, prolactin or hGH-V. The invention also describes a method for
CC diagnosing a probable abnormality of placental vascularisation during
CC pregnancy. The peptides can be used for treating an angiogenic disease in
CC a subject, for inhibiting tumour formation or growth in a patient or for
CC modulating vascularisation of a patient's placenta. In particular, the
CC peptides can be used for preventing or treating e.g. malignant tumours,
CC angiofibroma, arteriovenous malformation, arthritic such as rheumatoid
CC arthritis, atherosclerotic plaques, corneal graft neovascularisation,
CC delayed wound healing, proliferative retinopathy such as diabetic
CC retinopathy, macular degeneration, granulations such as those occurring
CC in haemophilic joints, inappropriate vascularisation in wound healing
CC such as hypertrophic scars or keloid scars, neovascular glaucoma, ocular
CC tumour, uveitis, non-union fractures, Osler-Weber syndrome, psoriasis,
CC pyogenic glaucoma, retrolental fibroplasia, scleroderma, solid tumours,
CC Kaposi's sarcoma, trachoma, vascular adhesions, chronic varicose ulcers,
CC leukaemia, and reproductive disorders such as follicular and luteal cysts
CC and choriocarcinoma. They can also be used as contraceptive agents. DNA
CC encoding the peptides can be used in gene therapy. The measurement of
CC abnormal levels of N-terminal fragments of hGH, hGH-V, prolactin or hPL
CC can be used in assays for impairment of vascular development associated
CC with pre-eclampsia, intrauterine growth retardation, and placental
CC dysfunction.
XX
SQ Sequence 192 AA;

Query Match 95.4%; Score 83; DB 20; Length 192;
Best Local Similarity 93.8%; Pred. No. 4.8e-05;
Matches 15; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 YLRIVQCRSVEGSCGF 16
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Db 177 flrivqcrsvegscgf 192

Search completed: July 10, 2002, 08:25:19
Job time: 191 sec